

33. The artificially constructed hybrid cytokine dimer of claim 32 further comprising a low molecular weight oligosaccharide linker joining said IL-7 and the  $\beta$ -chain of HGF.

34. The artificially constructed hybrid cytokine dimer of claim 33 wherein said low molecular weight oligosaccharide is heparin sulfate-derived oligosaccharide.

35. The artificially constructed hybrid cytokine dimer of claim 34 wherein said heparin sulfate has a molecular weight of less than about 3000kD.

a) 36 An artificially constructed hybrid cytokine complex comprising the complexed bioactive portions of interleukin-7 and the beta chain of HGF connected with a flexible linker selected from the group consisting of disulfide bridges, heparin and heparan sulfate derived oligosaccharides, bifunctional and chemical cross-linkers and polypeptide linkers, wherein the hybrid cytokine complex has the properties of PPBSF but is not isolated from a natural source.

37. The artificially constructed hybrid cytokine complex of claim 36 wherein said flexible linker is a low molecular weight oligosaccharide.

38. The artificially constructed hybrid cytokine of claim 37 wherein said oligosaccharide is a heparin sulfate-derived oligosaccharide.

39 The artificially constructed hybrid cytokine of claim 38 wherein said heparin sulfate-derived oligosaccharide has a molecular weight of less than about 3000kD.

40. A biological preparation comprising an artificially constructed hybrid cytokine complex according to claim 36 and a pharmaceutically acceptable carrier.

41. A method of treating disorders of T-lymphocytes and B-lymphocytes comprising administering to a human or animal in need of such treatment a therapeutically effective amount of the biological preparation according to claim 40.

42. A method of treating hematopoietic disorders comprising administering to a human or animal in need of such treatment a therapeutically effective amount of the biological preparation according to claim 40.

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43. A method of treating immunodeficiency disorders which comprises administering to a human or animal in need of such treatment a therapeutically effective amount of the biological preparation according to claim 40

44. A method of treating leukemia which comprises administering to a human or animal in need of such treatment a therapeutically effective amount of the biological preparation according to claim 40.

45. A process for producing a hybrid cytokine heterodimer of IL-7 and the  $\beta$ -chain of HGF which comprises

(a) obtaining the recombinantly-derived  $\beta$ -chain of hepatocyte growth factor (HGF) by:

(1) cloning HGF $\beta$  cDNA into mammalian or prokaryotic

expression vectors and transfecting or transforming the vectors into mammalian or prokaryotic cells;

(2) growing the transfected or transformed cells *in vitro*;

(3) isolating purified  $\beta$ -chain of hepatocyte growth factor (HGF) by extraction from the cell culture;

and

(b) obtaining IL-7 from a recombinant or natural source;

(c) linking the recombinantly-derived  $\beta$ -chain of hepatocyte growth factor (HGF) of step (a) with the IL-7 of step (b) by way of a low molecular weight oligosaccharide linker.

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46. A bimolecular protein complex (IL-7HGF $\beta$ ) comprising the artificially constructed hybrid cytokine complex according to claim 36 which supports the proliferation and differentiation of pre-pro- $\beta$ -cells.

47. A bimolecular protein complex (IL-7/HGF $\beta$ ) according to claim 46 wherein said flexible linker is a low molecular weight oligosaccharide.

48. A bimolecular protein complex (IL-7HGF $\beta$ ) according to claim 47 wherein said oligosaccharide is a heparin sulfate-derived oligosaccharide.

49. A bimolecular protein complex (IL-7/HGF $\beta$ ) according to claim 48 wherein said heparin sulfate-derived oligosaccharide has a molecular weight of less than about 3000kD.

50. A method of forming a bimolecular protein complex (IL-7/HGF $\beta$ ) which supports the proliferation of pre-pro- $\beta$ cells comprising linking IL-7 or a homologous peptide thereof with HGF $\beta$  or a homologous peptide thereof with a low molecular weight oligosaccharide.

51. The method of claim 50 wherein said homologous peptide is a member selected from the group consisting of substitution analogs, addition analogs and deletion analogs.

52. The method of claim 50 wherein said homologous peptide is a member selected from the group consisting of heterodimeric and multimeric cytokine complexes containing IL-7 and/or HGH ( $\alpha$  and/or  $\beta$ -chains).

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#### REMARKS

The instant invention is directed to a hybrid cytokine consisting of IL-7 and the  $\beta$ -chain of the hepatocyte growth factor. This heterodimer constitutes a pre-pro-B cell growth stimulating factor (PPBSF) which selectively induces proliferation and differentiation of pre-pro-B cells. The applicants have further found that in the presence of a low molecular weight oligosaccharide such as a heparin sulfate-derived oligosacchride the HGF $\beta$  complexes with the IL-7 to form a biologically active heterodimer having the properties of PPBSF. PPBSF as produced by the inventors is a hybrid cytokine consisting of the complexed bioactive portions of two independently generated cytokines. As already noted